

In re Application of  
DARREN R. SHAFREN  
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**Amendments to the Claims:**

Please cancel claim 63 without prejudice.

Please amend claims 1-62 as follows.

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A method for ~~treatment of~~ treating abnormal cells in a mammal, ~~the method comprising treating~~ administering to the mammal with an effective amount of virus selected from echo viruses, and modified forms and combinations thereof, which ~~recognise~~ recognize  $\alpha_2\beta_1$  for infectivity of the cells such that at least ~~some~~ one of the cells are killed by the virus.

2. (Currently Amended) [[A]] The method according to claim 1 further comprising subjecting the mammal to ~~a number of treatments~~ more than one treatment with the virus, and wherein the virus in each of the treatments is the same or different.

3. (Currently Amended) [[A]] The method according to claim 1 wherein the virus comprises an echovirus serotype or a modified form thereof.

4. (Currently Amended) [[A]] The method according to claim 3 wherein the virus is ~~selected from the group consisting of~~ EV1 and or EV8.

5. (Currently Amended) [[A]] The method according to claim 3 wherein the virus is a modified echovirus.

6. (Currently Amended) [[A]] The method according to claim 5 wherein the virus has been modified to enhance ability of the virus to infect the abnormal cells.

7. (Currently Amended) [[A]] The method according to claim 5 ~~or 6~~ wherein the modified echovirus is a modified form of ~~an echovirus selected from a group consisting of~~ EV1 ~~and or~~ EV8.

8. (Currently Amended) [[A]] The method according to ~~any one of claim~~[[s]] 1 ~~to 7~~ wherein the virus is administered to the mammal in combination with a ~~further~~ second virus which infects the abnormal cells.

9. (Currently Amended) [[A]] The method according to claim 8 wherein the abnormal cells express ICAM-1 and the ~~further~~ second virus ~~recognises~~ recognizes ICAM-1 for infectivity of the abnormal cells.

10. (Currently Amended) [[A]] The method according to claim 9 wherein the ~~further~~ second virus is a Coxsackievirus or a modified form thereof.

11. (Currently Amended) [[A]] The method according to claim 10 wherein the Coxsackievirus is a Coxsackievirus serotype selected from A13, A1 5, A1 8 and A21.

12. (Currently Amended) [[A]] The method according to ~~any one of claim~~[[s]] 1 ~~to 11~~ wherein the abnormal cells are cancer cells.

13. (Currently Amended) [[A]] The method according to claim 12 wherein the cancer cells are ~~cells of a cancer selected from a group consisting of~~ ovarian cancer cells, melanoma cells, prostate cancer cells, breast cancer cells, pancreatic cancer cells, colon cancer cells ~~and or~~ colorectal cancer cells, or are cells that have spread from ovarian cancer, melanoma, prostate cancer, breast cancer, pancreatic cancer, colon cancer or colorectal cancer.

14. (Currently Amended) [[A]] The method according to ~~any one of claim~~[[s]] 1 ~~to 13~~ wherein the abnormal cells have up-regulated expression of  $\alpha_2\beta_1$ .

15. (Currently Amended) [[A]] The method according to ~~any one of claim~~[[s]] 1 to 14 wherein the virus is administered topically, systemically or intratumorally to the mammal.

16. (Currently Amended) A method of screening a sample of abnormal cells from a mammal for susceptibility to virus induced cell death to evaluate administering virus to the mammal for treatment of the abnormal cells, the method comprising:

(a) ~~providing the sample of the abnormal cells;~~

(((b))a) treating contacting the cells with the a virus for a period of time sufficient to allow infection of the cells by the virus; and

(((c))b) determining whether the virus has infected the cells and caused death of at least ~~some one~~ one of the abnormal cells;

wherein the virus is selected from echo viruses, and modified forms and combinations thereof, which ~~recognise~~ recognize  $\alpha_2\beta_1$  for infectivity of the abnormal cells.

17. (Currently Amended) [[A]] The method according to claim 16 wherein the virus ~~comprises~~ is an echovirus serotype or a modified form thereof.

18. (Currently Amended) [[A]] The method according to claim 16 wherein the virus is ~~selected from a group consisting of EV1 and or~~ EV8.

19. (Currently Amended) [[A]] The method according to claim 17 wherein the virus is a modified echovirus.

20. (Currently Amended) [[A]] The method according to claim 19 wherein the virus has been modified to enhance ability of the virus to infect the abnormal cells.

21. (Currently Amended) [[A]] The method according to claim 19 ~~or 20~~ wherein the modified echovirus is a modified form of an ~~echovirus selected from a group consisting of EV1 and or~~ EV8.

22. (Currently Amended) [[A]] The method according to ~~any one of claim~~[[s]] 16 to 21 further comprising comparing the ability of the virus to infect the cells and cause death of the cells, ~~to with a different the ability of a second virus that recognizes  $\alpha_2\beta_1$  for infectivity of the cells~~, subjected to steps ~~(b) and (e)~~ (a) and (b) ~~utilising~~ utilizing another sample of the cells, to infect the cells and cause death and ~~which recognises  $\alpha_2\beta_1$  for infectivity of the cells~~.

23. (Currently Amended) [[A]] The method according to claim 22 wherein the ~~different~~ second virus is a different echovirus or modified form thereof.

24. (Currently Amended) [[A]] The method according to ~~any one of claim~~[[s]] 16 to 23 wherein the cells are cancer cells.

25. (Currently Amended) [[A]] The method according to claim 24 wherein the cancer cells are ~~cells of a cancer selected from a group consisting of ovarian cancer~~ cells, melanoma cells, prostate cancer cells, breast cancer cells, pancreatic cancer cells, colon cancer cells and or colorectal cancer cells, or are cells that have spread from ovarian cancer, melanoma, prostate cancer, breast cancer, pancreatic cancer, colon cancer or colorectal cancer.

26. (Currently Amended) A method of screening a virus for ability to infect and cause death of abnormal cells from a mammal to evaluate administering the virus to the mammal for treatment of the abnormal cells, the method comprising:

(a) ~~selecting the virus;~~

(((b))a) ~~treating~~ contacting a sample of the abnormal cells from the mammal with ~~the~~ a virus for a period of time sufficient to allow infection of the cells by the virus; and

(((c))b) determining whether the virus has infected and caused death of at least ~~some~~ one of the abnormal cells;

wherein the virus is selected from echoviruses and modified forms thereof, which ~~recognise~~ recognize  $\alpha_2\beta_1$  for infectivity of the abnormal cells.

27. (Currently Amended) [[A]] The method according to claim 26 wherein the virus ~~comprises~~ is an echovirus serotype or a modified form thereof.

28. (Currently Amended) [[A]] The method according to claim 26 wherein the virus is ~~selected from a group consisting of EV1 and~~ or EV8.

29. (Currently Amended) [[A]] The method according to claim 27 wherein the virus is a modified echovirus.

30. (Currently Amended) [[A]] The method according to claim 29 wherein the virus has been modified to enhance the ability of the virus to infect the abnormal cells.

31. (Currently Amended) [[A]] The method according to claim 29 ~~or 30~~ wherein the modified echovirus is a modified form of ~~an echovirus selected from a group consisting of~~ EV1 ~~and~~ or EV8.

32. (Currently Amended) [[A]] The method according to ~~any one of claim[[s]] 26 to 31~~ further comprising comparing ability of the virus to infect and cause death of the cells, to the ability of with a different second virus that recognizes  $\alpha_2\beta_1$  for infectivity of the cells, subjected to steps ~~(b) and (c)~~ utilising (a) and (b) utilizing another sample of the cells, to infect the cells and cause death ~~and which recognizes  $\alpha_2\beta_1$  for infectivity of the cells.~~

33. (Currently Amended) [[A]] The method according to claim 32 wherein the ~~different~~ second virus is a different echovirus or modified form thereof.

34. (Currently Amended) [[A]] The method according to ~~any one of claim[[s]] 26 to 33~~ wherein the abnormal cells are cancer cells.

35. (Currently Amended) [[A]] The method according to claim 34 wherein the cancer cells are ~~cells of a cancer selected from a group consisting of ovarian cancer cells, melanoma cells, prostate cancer cells, breast cancer cells, pancreatic cancer cells, colon cancer cells and or colorectal cancer cells, or are cells that have spread from ovarian cancer, melanoma, prostate cancer, breast cancer, pancreatic cancer, colon cancer or colorectal cancer.~~

36. (Currently Amended) A method for inducing an immune response in a mammal against abnormal cells expressing  $\alpha_2\beta_1$ , the method comprising infecting abnormal cells in the mammal with a virus selected from the group consisting of echoviruses, and modified forms thereof, and combinations thereof, whereby thereby causing lysis of at least some one of the cells is caused and inducing an immune response in the mammal against the abnormal cells.

37. (Currently Amended) [[A]] The method according to claim 36 wherein the virus comprises is an echovirus serotype of or modified form thereof.

38. (Currently Amended) [[A]] The method according to claim 37 wherein the virus is selected from the group consisting of EV1 and or EV8.

39. (Currently Amended) [[A]] The method according to claim 37 wherein the virus is a modified echovirus.

40. (Currently Amended) [[A]] The method according to claim 39 wherein the virus has been modified to enhance ability of the virus to infect the abnormal cells.

41. (Currently Amended) [[A]] The method according to claim 39 or 30 wherein the modified echovirus is a modified form of an echovirus selected from a group consisting of EV1 and or EV8.

42. (Currently Amended) [[A]] The method according to ~~any one of claim~~[[s]] 36 to 41 wherein the abnormal cells have up-regulated expression of  $\alpha_2\beta_1$ .

43. (Currently Amended) [[A]] The method according to ~~any one of claim~~[[s]] 36 to 42 wherein the virus is administered to the mammal in combination with a further second virus which infects the abnormal cells.

44. (Currently Amended) [[A]] The method according to claim 43 wherein the abnormal cells express ICAM-1 and the further second virus ~~recognises~~ recognizes ICAM-1 for infectivity of the abnormal cells.

45. (Currently Amended) [[A]] The method according to claim 44 wherein the further second virus is a Cocksackievirus or modified form thereof.

46. (Currently Amended) [[A]] The method according to claim 45 wherein the Cocksackievirus is a Cocksackievirus serotype selected from A13, A15, A18 and A21.

47. (Currently Amended) [[A]] The method according to ~~any one of claim~~[[s]] 36 to 46 wherein the abnormal cells are cancer cells.

48. (Currently Amended) [[A]] The method according to claim 47 wherein the cancer cells are ~~cells of a cancer selected from a group consisting of~~ ovarian cancer cells, melanoma cells, prostate cancer cells, breast cancer cells, pancreatic cancer cells, colon cancer cells and or colorectal cancer cells, or are cells that have spread from ovarian cancer, melanoma, prostate cancer, breast cancer, pancreatic cancer, colon cancer or colorectal cancer.

49. (Currently Amended) [[A]] The method according to ~~any one of claim~~[[s]] 36 to 48 wherein the virus is administered topically, systemically or intratumorally to the mammal.

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50. (Currently Amended) A pharmaceutical composition for treating abnormal cells in a mammal, comprising an inoculant for generating virus to treat the cells such that at least ~~some one~~ one of the cells ~~are is~~ killed by the virus, ~~and together with~~ a pharmaceutically acceptable carrier, wherein the virus recognizes  $\alpha_2\beta_1$  for infectivity of the cells and is selected from echoviruses, ~~and modified forms thereof, which recognise~~ modified forms thereof, and combinations thereof, ~~which recognise~~  $\alpha_2\beta_1$  for infectivity of the cells.

51. (Currently Amended) [[A]] The pharmaceutical composition according to claim 50 wherein the virus ~~comprises~~ is an echovirus serotype or modified form thereof.

52. (Currently Amended) [[A]] The pharmaceutical composition according to claim 51 wherein the virus is ~~selected from the group consisting of EV1 and or~~ selected from the group consisting of EV1 and or EV8.

53. (Currently Amended) [[A]] The pharmaceutical composition according to claim 49 wherein the virus is a modified echovirus.

54. (Currently Amended) [[A]] The pharmaceutical composition according to claim 51 wherein the virus has been modified to enhance ability of the virus to infect the abnormal cells.

55. (Currently Amended) [[A]] The pharmaceutical composition according to claim 53 ~~or 54~~ wherein the modified echovirus is a modified form of ~~an echovirus selected from a group consisting of EV1 and or~~ an echovirus selected from the group consisting of EV1 and or EV8.

56. (Currently Amended) [[A]] The pharmaceutical composition according to ~~any one of claim[[s]] 50 to 55~~ wherein the abnormal cells are cancer cells.

57. (Currently Amended) [[A]] The pharmaceutical composition according to ~~any one of claim[[s]] 50 to 56~~ wherein the pharmaceutical composition is for topical administration or injection.



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58. (Currently Amended) An applicator for applying an inoculant to a mammal for generating a virus to treat abnormal cells in the mammal, wherein the applicator comprises a region impregnated with the inoculant ~~mammal such that the inoculant is in contact with the mammal~~, and the virus recognizes  $\alpha_2\beta_1$  for infectivity of the cells and is selected from echoviruses, ~~and modified forms thereof, which recognise  $\alpha_2\beta_1$  for infectivity of the cells.~~

59. (Currently Amended) ~~[[An]]~~ The applicator according to claim 58 wherein the region impregnated with the ~~virus~~ inoculant comprises padding or wadding for ~~being held~~ holding the inoculant in contact with the mammal.

60. (Currently Amended) ~~[[An]]~~ The applicator according to claim 58 ~~or 59~~ wherein the abnormal cells are abnormal skin cells and the applicator further comprises one or more adhesive surfaces for adhering to skin of the mammal.

61. (Currently Amended) ~~[[An]]~~ The applicator according to ~~any one of claim[[s]]~~ 58 to 60 wherein the region is in the form of a patch or sticking plaster.

62. (Currently Amended) ~~Use of an inoculant for generating virus in the manufacture of medicament~~ A method for inducing an immune response against abnormal cells in a mammal~~[[,]]~~ comprising contacting the applicator of claim 58 with abnormal cells of a mammal, and allowing the virus to lyse at least one of the abnormal cells, thereby inducing an immune response against abnormal cells in the mammal ~~where the virus is selected from echovirus, and modified forms and combinations thereof, which recognize  $\alpha_2\beta_1$  for infectivity of the abnormal cells.~~

63. (Canceled)